REMARKS

The Office Action mailed December 15, 2004 has been carefully reviewed and the foregoing amendments are made in response thereto. In view of the amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

New claims 174-177 have been added. Support for claim 174 may be found in figure 13 and on page 17 lines 1- 21. Support for new claims 175 and 176 may be found on page 16, lines 2-3. Support for new claim 177 may be found on page 16, lines 17-18.

Objection to the Claims

Claim 39 was objected to because of a typographical error resulting in the inclusion of an extra comma. Applicants have amended the claim to delete the comma.

Claims 57 and 58 were objected to because of the use of the generic term nucleic acid combined with the phrase "only DNA duplexes". The claim has been amended to clarify that DNA target is captured and the single stranded portion of the captured target is digested with the single stranded DNA nuclease to form double stranded DNA duplexes of target DNA and the oligonucleotide probes.

Rejections under 35 USC § 103(a)

The Examiner has maintained the rejection of Claims 39-53 over McCasky Feazel *et al.* (U.S. Patent No. 6,100,030) in view of DeRisis et al. (Science 278:680-686, 1997) and Moyer et al. (Applied and Environmental Microbiology 62:2501-2507, 1996).

On page 4 of the office action the Examiner asserts that the claims do not recite a limitation that the array is designed to interrogate polymorphism in the amplified sample after complexity reduction. Applicants have amended claim 39 to clarify the connection between the prediction of the polymorphisms that will be reproducibly amplified and the probes of the array. A computer is used to predict the polymorphisms that will be present on fragments that will be amplified. The probes of the array are selected to interrogate the genotype of a subset of those polymorphisms. The computer simulation is not simply a prediction of what fragments will result when a sample is digested with a given

restriction enzyme, as taught in Moyer, but also a prediction of which of those fragments are within the size range that will be amplified by PCR and which of those contain a polymorphism. The reduction in complexity should be reproducible and the presence or absence of the polymorphism should not alter the amplification of the fragment under the selected complexity reduction method. This is in contrast to McCasky Feazel et al. which teaches identification of markers based on polymorphisms that result in differential amplification depending on which variant is present.

Applicants respectfully disagree with the Examiner's assertion that the methods provide an automation of the manual process disclosed in McCasky Feazel et al. and that both methods accomplish the same result. The set of polymorphisms that is suitable for analysis by the methods of McCasky Feazel is distinct from the set of polymorphisms that is suitable for analysis by the presently claimed methods. McCasky Feazel et al. teach methods to genotype polymorphisms that are identifiable through differential amplification. This is a limited subset of the polymorphisms present in the genome. To be detected by the AFLP methods taught in McCasky Feazel et al. a polymorphism must meet one of several criteria that result in an empirically detectable alteration in amplification. The polymorphisms that can be identified by this method include polymorphisms within restriction sites, polymorphisms within a few bases of a restriction site (which can be detected using a selective primer for amplification) and polymorphisms that result in large insertions or deletions within a restriction fragment so that the resulting fragments can be distinguished in size by gel electrophoresis. In contrast the presently claimed invention provides for the detection of single nucleotide polymorphisms located within fragments; polymorphisms that do not alter the amplification of the fragment they are within. To provide for reproducible amplification the polymorphisms of the present invention are not within the restriction site of the enzyme used for fragmentation and do not alter the size of the fragment significantly. Reconsideration and withdrawal of the rejection of claims 39-53 is respectfully requested.

CONCLUSION

For the foregoing reasons, Applicants believe all the pending claims are now in condition for allowance and should be passed to issue. Please deduct any additional fees

from, or credit any overpayment to the above-noted Deposit Account. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5768.

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Respectfully submitted,

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